Title: METHODS FOR TREATING CANCER BY INHIBITING WNT SIGNALING Inventors: Bia HE et al. – Filed: Herewith.

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Wnt-1 Ab H28 Æ MCF-7 SKBR-3 SW480 SA0S-2 LP-9 A549 69 8

Cell death after anti-Wnt Ab incubation (%)

F/G. /

Fraction of apoptotic cell death (%) after anti-Wnt antibody treatment

Cell Line	No Treatment	Control Ab	Anti-Wnt-1 Ab	Anti-Wnt-2 Ab
CCL-75 (normal lung)	0.9 ±0.3	3.8 ±2.3	5.8 ±2.1	2 ±1.1
H838 (lung cancer)	1.7 ±0.8	3.1 ±3.0	28.4 ±4.6	58.3 ±8.1
H460 (lung cancer)	0.6 ±0.3	12.7 ±7.0	83.8 ±5.6	90.7 ±6.5
A549 (lung cancer)	0.3 ±0.1	4.9 ±3.0	84.7 ±3.3	82.3 ±4.5
MCF-7 (breast cancer)	0.7 ±0.4	1.6 ±0.7	56.7 ±3.9	47.2 ±4.2
SKBR-3 (breast cancer)	0.4 ±0.1	5.8 ±1.3	67.9 ±6.1	56.4 ±4.8
SW-480 (colon cancer)	5.9 ±0.8	14.6 ±4.6	43.3 ±4.4	48.9 ±5.2
SAOS-2 (sarcoma)	1.1 ±0.4	4.2 ±1.6	20.0 ±3.2	16.5 ±1.0
LP-9 (normal mesothelial)	2.3 ±1.1	5.1 ±2.7	4.1.±1.5	6.2 ±2.6
REN (mesothelioma)	13.6 ±2.4	15.2 ±6.5	89.6 ±3.8	81.4 ±8.4
H28 (mesothelioma)	6.6 ±3.5	12.4 ±7.4	68.7 ±5.8	41.3 ±6.6

FIG. 2

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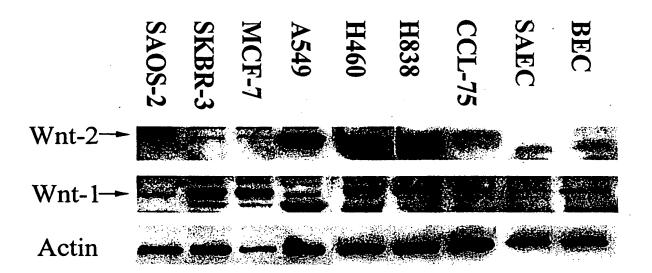


FIG. 3A

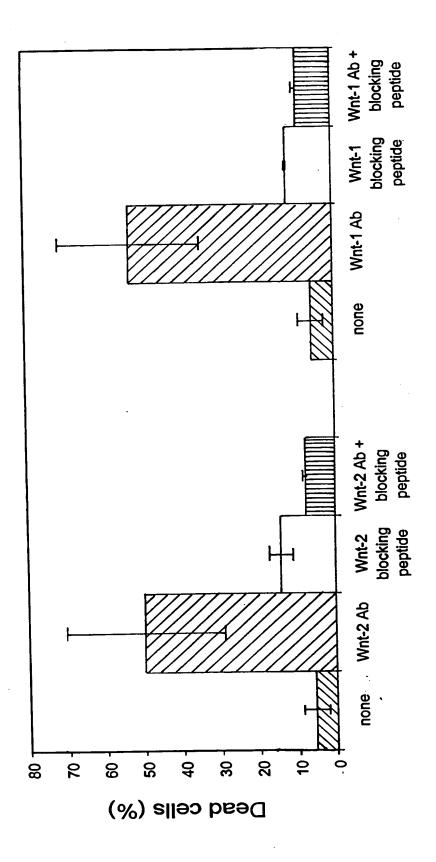
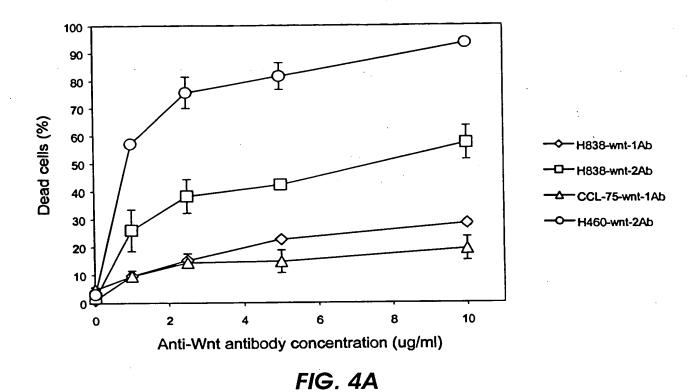
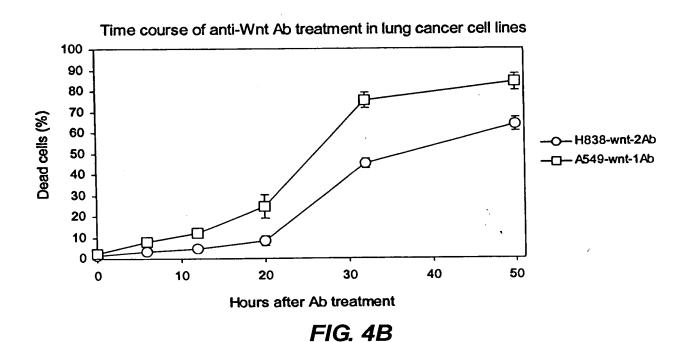


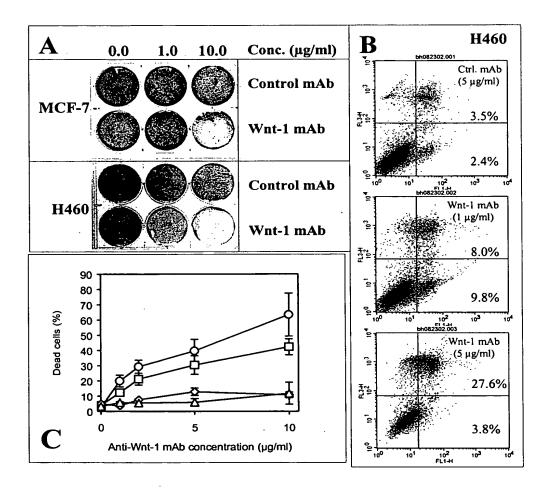
FIG. 3B

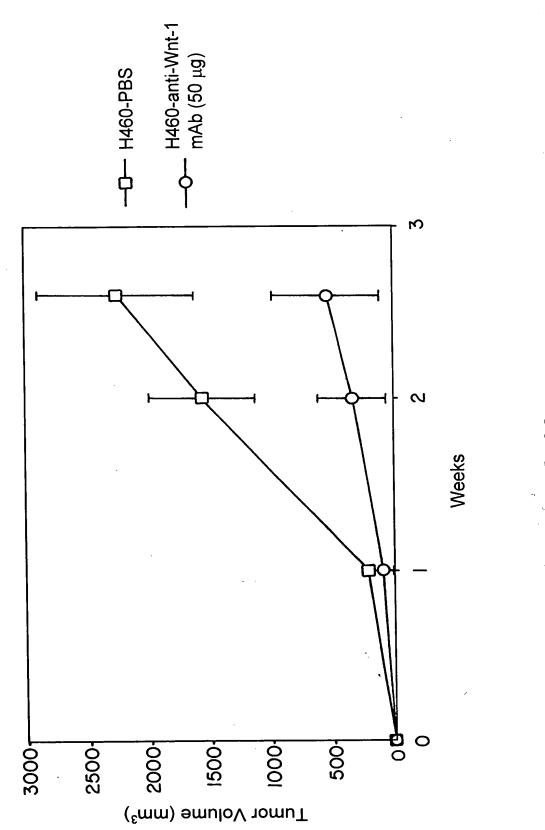


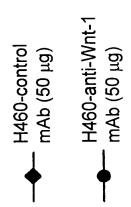


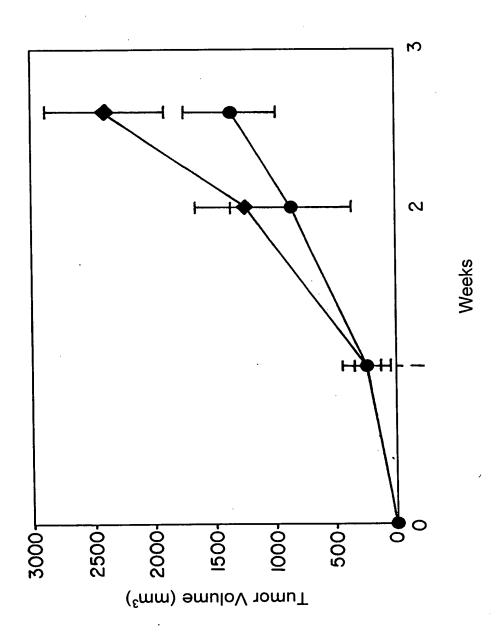
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FIGURE 5

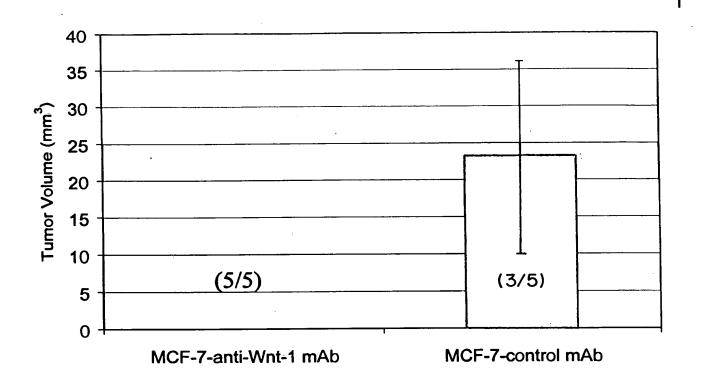








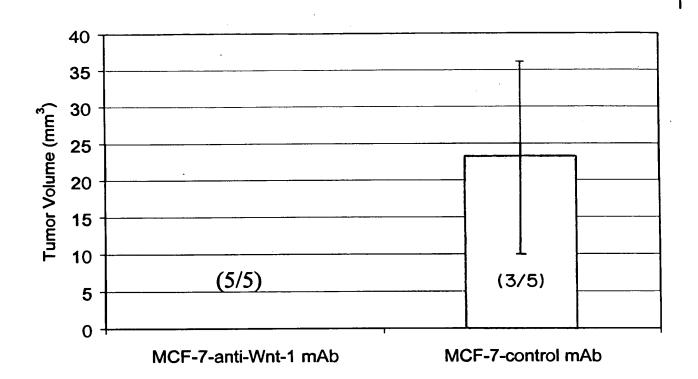
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in vivo study on breast cancer. Tumor volume is shown after 3 weeks treatment with anti-Wnt-1 monoclonal antibody and control monoclonal antibody. 5 animals are in each group. None of the animals grows tumor after anti-Wnt-1 mAb injection, but three out of five animals grow tumor in the control group. (I.P. injection was done once weekly one week after inoculation of the MCF-7 cells)

FIG. 6C

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in vivo study on breast cancer. Tumor volume is shown after 3 weeks treatment with anti-Wnt-1 monoclonal antibody and control monoclonal antibody. 5 animals are in each group. None of the animals grows tumor after anti-Wnt-1 mAb injection, but three out of five animals grow tumor in the control group. (I.P. injection was done once weekly one week after inoculation of the MCF-7 cells)

FIG. 6C

a anti-WNT1 antibody (Seq ID Figure 7

1) CDR and FR region (light chain kappa) amino acid sequence of No:4)

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1y22W11kRs CTC AAC ATC CAT CCT GTG GAG GA MGT 115 S T x R R G E B 1y22W11kRs AGC ACG TTX CGG AGG GGG GAG CC 2) CDR and FR region (light chain No:9)		1 D I V L ly23w2lkRs GAC ATT GTĠ CTG		ly23w21kRs	45 K P G Q ly23w2lkRs AAA CCA GGA CAG	

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TGC AGC CDR3 1y23w2lkRs ACA TTA GGG AGC TTA CAC GTT ACG GAG GGG GGA CCA AGC TGA AAA AAC GG JGC 80 Q GGA GGA TCC ATG CCT TCA CAC CTT MGT

a anti-WNT1 antibody (Seg ID No:4) 3) CDR and FR region (heavy chain IgG1) amino acid sequence of

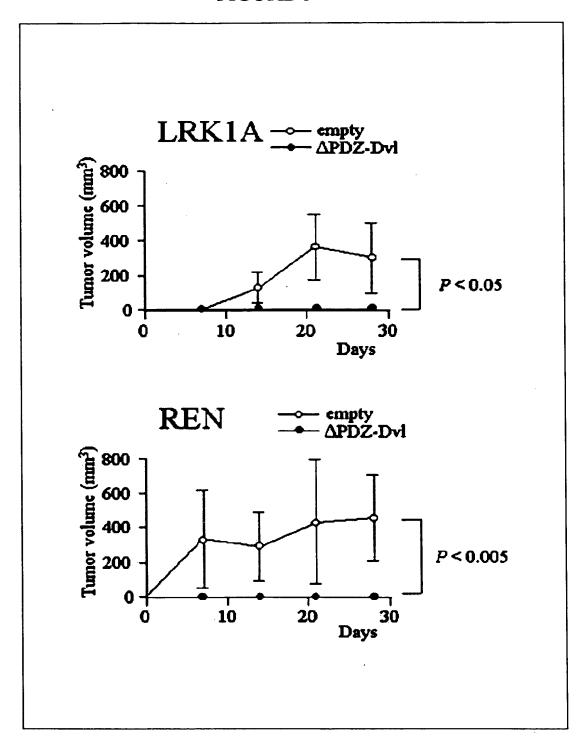
GATTCACITITAATACCIACGCC......AIGAACIGGGICCGCCAGGCICCAGGAAAGGGITIGGAAIGGGI TGCTCGCATAAGAACTAGACGTTATAATTCTGCAACATATTATGCCGATTCTGTGAAA....GACAGGTTCACCATCTCC XGTTXCAGCCTGXAGGAGTCXGGTGGA....GGATTGGTGCAGCCTAAAGGGTCATTGAAACTCTCATGTGCAGCCTCTG AGAGATGATTCACGGGGCATGCTCTATCTGCAAATGAACAACTTGAAAACTGAGGACACAGCCATGTATTACTGTGTGA (Sed ID No:9) a anti-WNT2 antibody 4) CDR and FR region (heavy chain IgG1) amino acid sequence of

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ч	:		ာ TgC	ഥ	45 R AGA	1	Y TAC	M
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FIGURE 8



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FIGURE 9

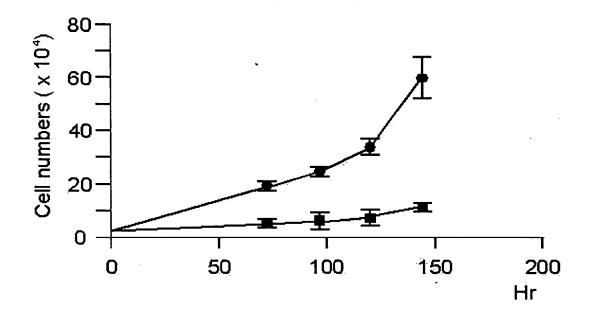


Figure 10. Over-expression of Wnt signal antagonist (FRP or DKK) induces apoptosis in cancer cell line MS-1

